REMARKS

Applicant's attorney wishes to thank both Examiner Snedden and SPE Weber for the careful consideration given this case, and the courteous interview of February 8, 2005. For the Examiner's convenience, included with this response is a copy of the Interview Summary from said interview. As was discussed and agreed upon during the interview, claims commensurate in scope with those presented herein are patentable over both U.S. Pat. No. 6,608,026 to Wang et al. ("Wang") and U.S. Pub. No. 2002/0132786 to Alnemri ("Alnemri"), as well as the cited prior art. Notice to such effect is respectfully requested.

Before turning to the substantive aspects of this response, a number of informalities will be addressed. Initially, as was noted during the interview, the provisional application number cited in the oath, the related data portion of the specification, and in the priority claim of the application is in fact a typographical error that appears to have inadvertently been introduced at the time of filing the non-provisional. Instead of U.S. Provisional App. No. 60/236,574, the correct Provisional Application No. is 60/236,474. The specification has been amended accordingly and a substitute Oath and Declaration is submitted herewith.

Additionally, in order to be fully responsive to the Office Action, Applicant affirms the election with traverse to prosecute the invention of Group I and the election of AVPI as the species. However, Applicant respectfully points out that due to the agreement reached during the interview, a portion of the restriction requirement and species election should be revisited and withdrawn. Specifically, claim 7 as a non-elected species and the restriction of claims 11, 12, 18, 19 and 20 (Group V) should be withdrawn in light of the agreement to include the elements of claim 5 in claim 1. Furthermore, claims 13-17 (Group VI) as method claims should be rejoined in light of re Ochiai (USPQ Fed. Cir. 1995) as the composition of matter claims are in condition for allowance. Applicant has cancelled claim 12 as it depended from claim 8. Accordingly, Applicant respectfully requests that claims 1-4, 6, 7, 11 and 13-20 be passed to issue.

As was discussed and agreed upon in the interview, neither the AVPI peptide described *per se* in Wang, nor Alnemri's teaching of a functional equivalent of a Smac peptide anticipate or make obvious the presently claimed invention. Wang presents data in Table 4 that purports to show that AV is the critical component in enhancing apoptosis (hence the "AV-

peptoid") by purportedly showing IAP Binding of representative AV peptoids, including AV, AVP, and AVPI among others. As was discussed during the interview, Wang's disclosure when reviewed in its entirety has little import to one ordinarily skilled in the art in arriving at Applicant's presently claimed invention. Wang provides little more than an invitation to experiment with AV peptoids. Applicant, on the other hand, shows for the first time that a tetrapetide (e.g. AVPI) is functional in enhancing apoptosis and demonstrates structurally the interaction of the tetrapeptide region of Smac with the BIR3 domain of XIAP via a high resolution crystal structure of a complex of Smac with the BIR3 domain of XIAP (see Fig. 1-10 and pp. 21-22 of Applicant's specifications). Simply put, Applicant provided both the structure and function for rational design of compounds having the binding functionality of Smac or homologs thereof.

As was discussed in the interview and as is evidenced from Applicant's Nature publication[1], Applicant knew that a Del-1 mutant had no activity, that a Del-4 mutant had reduced activity, that a seven amino peptide can activate procaspase-3 activation, and that shorter peptides could possess similar activities. However, until Applicant elucidated the crystal structure showing the interaction of Smac and XIAP, one skilled in the art would not know what tertiary structure to mimic, and would be guessing, at best, as to the necessary elements of a peptidomimetic. Applicant demonstrated conclusively that a mimetic of the claimed sequence would be a suitable agent to enhance apoptosis.

The amended claims are commensurate in scope with a fundamental and important discovery by Applicant that a molecule that mimics the tertiary binding structure of Smac would be useful as composition or compound to inhibit IAP. Applicant demonstrated the importance of the BIR3 domain of XIAP, and provided a description of the suitable mimetics (see, e.g., p. 16, line 5; p. 17, line 31). To further clarify the presently claimed invention, the claims specify that the claimed peptidomimetic is capable of binding to a BIR-3 domain of an IAP, and further that the peptidomimetic includes a modified amino acid, a modified peptide bond, or a non-peptide portion.

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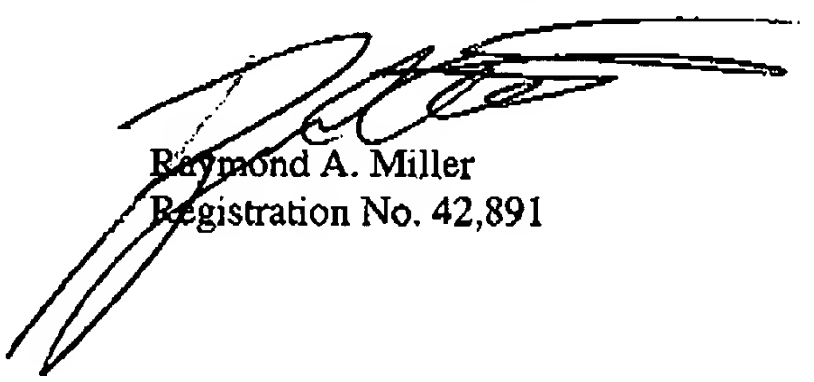
[1] A manuscript copy of the Nature article is provided for the Examiner's convenient reference. The article was submitted to Nature on July 4, 2000; on July 21, 2000, the Article was accepted; and on August 24, the Article was published in Nature.

In view of the remarks presented above, it is believed that the claims 1-4, 6 and 18 are in condition for final allowance and notice to such effect is respectfully requested. Additionally, Applicant respectfully requests that claims 7, 11 and 13-17, 19 and 20 be rejoined and given final allowance.

Although Applicant believes no fees, other than the fees for the additional claims are due, the Commissioner is hereby authorized to charge deposit account No. 50-0436 for any fees that may be due in connection with this response. Should the Examiner have any questions regarding these remarks, the Examiner is invited to initiate a telephone conference with the undersigned.

Respectfully Submitted,



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